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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/583,056	03/16/2007	Katherine S. Bowdish	ALEX-P01-112	8249

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EXAMINER	
EWOLDT, GERALD R	

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1644	

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09/30/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/583,056	BOWDISH ET AL.	
	Examiner	Art Unit	
	G. R. Ewoldt, Ph.D.	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 June 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20 and 31-47* is/are pending in the application.

4a) Of the above claim(s) *10,11,14-18,33,34 and 36-47* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-9,12,13,19,20,31,32 and 35* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date 3/7/07.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's election without traverse of Group I and the antibody species of SEQ ID NO:45, filed 6/08/09, is acknowledged.

Applicant argues that a specific method species election requirement should not be applied to Group I.

The specific method species election requirement was issued to differentiate antibodies intended as immune stimulators, viral entry blockers, and immunotoxins. Upon reconsideration however, the specific method species election requirement has been withdrawn.

2. Claims 10, 11, 14-18, 33, 34, and 36-47 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected inventions.

Claims 1-9, 12, 13, 19, 20, 31, 32, and 35 are under examination. Note the claims are under examination limited to the elected antibody species of SEQ ID NO:45.

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 1-9, 12, 13, 19, 20, 31, 32, and 35 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Specifically, there is no evidence of record that an antibody defined by a single CDR could bind DC-SIGN nor function as claimed in the dependent claims without undue experimentation.

The specification disclosure is insufficient to enable one skilled in the art to practice the invention as claimed without an undue amount of experimentation. Undue experimentation must

be considered in light of factors including: the breadth of the claims, the nature of the invention, the state of the prior art, the level of one of ordinary skill in the art, the level of predictability of the art, the amount of direction provided by the inventor, the existence of working examples, and the quantity of experimentation needed to make or use the invention, see *In re Wands*, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988).

In re Fisher, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970) states, "The amount of guidance or direction needed to enable the invention is inversely related to the amount of knowledge in the state of the art as well as the predictability in the art." "The "amount of guidance or direction" refers to that information in the application, as originally filed, that teaches exactly how to make or use the invention. The more that is known in the prior art about the nature of the invention, how to make, and how to use the invention, and the more predictable the art is, the less information needs to be explicitly stated in the specification. In contrast, if little is known in the prior art about the nature of the invention and the art is unpredictable, the specification would need more detail as to how to make and use the invention in order to be enabling" (MPEP 2164.03). The MPEP further states that physiological activity can be considered inherently unpredictable. With these teachings in mind, an enabling disclosure, commensurate in scope with the breadth of the claimed invention, is required.

The claims recite an antibody defined by the single 9 amino acid CDR of SEQ ID NO:45. Independent Claim 1 recites an antibody that need be only be 80% identical to SEQ ID NO:45, i.e., an antibody defined by just 8 amino acids. A review of the prior art reveals that such an antibody would not be expected to function as claimed, i.e., specifically bind DC-SIGN. See, for example, De Pascalis et al. (2002) wherein the authors teach that residues from all 6 CDRs participate in antigen binding, and then only when grafted onto particular frameworks. Lamminmaki et al. (2001) discloses similar findings. The authors teach that in a crystal structure of an exemplary antigen-antibody complex, while CDR_{H3} plays a prominent role in binding, all CDRs in the V_L also make contact with the antigen.

Regarding mutated antibodies with as little as 80% identity to the antibody of SEQ ID NO:45, a review of the prior art shows

that substituting amino acids within an antibody chain can be highly unpredictable and generally produces a non-functional antibody. See, for example, Chen et al. (1992). The reference teaches that when 46 *single* random point mutations were introduced into an antibody, 20 non-functional antibodies, 6 reduced-function antibodies, and no increased-function antibodies were produced. And note that these mutations were not limited to mutations in the critical CDR binding regions of the antibody (which would be expected to further adversely affect antigen binding).

Also note that the antibody of the dependent claims has been claimed by additional limitations that have not been demonstrated. For example, the antibody of Claims 5 and 6 has been claimed as a vaccine and the antibody of Claim 35 has been claimed as a therapeutic agent for treating cancer. These limitations raise the enablement bar even higher. Vaccines encompass the complete prevention of any disease for which an antigen has been identified (Claim 5) or the prevention or cure of cancer (Claim 6). Regarding the antibody of Claim 35, neither the antigens employed not the types of cancer to be treated are disclosed in the specification nor recited in the claims. Thus, the antibody should be able to provide an effective treatment for any type of cancer employing essentially any type of antigen. Clearly, an antibody claimed that broadly is not enabled by the instant specification nor the prior art. Regarding the antibody of Claim 19 that can effectively block the binding, infection, or transmission of numerous viruses, bacteria, and parasites, there is no such showing in the specification. While the prior art teaches that HIV may bind DC-SIGN (said binding facilitating the entry of the virus into CD4+ T cells) there is no nexus between said HIV binding and the binding, infection, or transmission of any of the other pathogens of the claim. And even as regards the binding of HIV by DC-SIGN, Geijtenbeek et al. (2000, IDS) teaches that the virus merely binds DC-SIGN and does not use the receptor to facilitate entry into DCs. Thus, the blocking of DC-SIGN with the antibody of the claims would not be expected to have any effect on the infection of the DCs expressing the DC-SIGN receptor. Accordingly, given that the specification provides no data regarding the treatment or prevention of any disease or condition, nor the effective blocking of the binding, infection, or transmission of the numerous viruses, bacteria, and parasites, of the claims, the specification fails to provide enablement commensurate in scope with the breadth of the claims.

For these reasons the antibody of the instant claims would require undue experimentation to produce and use as claimed.

5. Claims 1-9, 12, 13, 19, 20, 31, 32, and 35 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention.

Under *Vas-Cath, Inc. v. Mahurkar* , 19 USPQ2d 1111, 1117 (Fed. Cir. 1991), to satisfy the written description requirement, an applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in *possession* of the invention, and that the invention, in that context, is whatever is now claimed.

There is insufficient written description to show that Applicant was in possession of an isolated antibody that binds DC-SIGN described only by the CDR of SEQ ID NO:45. The specification discloses that the screened libraries comprised IgG1 and IgG2a antibodies that were screened for DC-SIGN binding. The sequences of these antibodies are not disclosed except as in Figure 4 wherein separate V_L and V_H are shown. It is not disclosed, however, which V_L form a functional antibody when paired with which V_H. Accordingly, the specification discloses only a function, i.e., DC-SIGN binding, but no common structure nor representative complete antibody species. Additionally, no antibodies comprising just the CDR of SEQ ID NO:45 are disclosed. Given these facts, one of skill in the art would conclude that the specification fails to adequately describe the antibody of the instant claims. See *Eli Lilly*, 119 F.3d 1559, 43 USPQ2d 1398.

6. No claim is allowed.

7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Dr. Gerald Ewoldt whose telephone number is (571) 272-0843. The examiner can normally be reached Monday through Thursday from 7:30 am to 5:30 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla, Ph.D. can be reached on (571) 272-0841.

8. **Please Note:** Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197.

/G.R. Ewoldt/
G.R. Ewoldt, Ph.D.
Primary Examiner
Technology Center 1600